UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,590	07/29/2003	Peter S. Lu	VITA-008	4993

24353 7590 02/16/2005

BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVENUE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 02/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/630,590	LU ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9-9-03, 5-21-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, and the species represented by Magi-I PDZ domain 2, in the reply filed on November 29, 2004 is acknowledged. It is first noted that the Applicant's arguments in traversal of the restriction between Groups I and II is found persuasive.

The Applicant argues in traversal of the species election that there would be no undue burden in the examination of all PDZ binding domain. However, as these different domains comprise different protein sequences from different proteins that perform different function, the unsupported assertion that there would be no undue burden is not found persuasive. In particular, because these different domains have different sequences, examination of each of the domains would require numerous and different searches, no one search of which would be capable of determining the patentability of all of the different potential PDZ domains.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 16-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 29, 2004.

3. Claims 1-15 are under consideration to the extent that they read on, or are generic to the elected inventions/species.

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

> This application is claiming the benefit of a prior filed nonprovisional application under 35 U.S.C. 120, 121, or 365(c). Copendency between the current application and the prior application is required.
>
> An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

The present application is attempting to claim priority to prior U.S. application 09/710,059, filed on November 10, 2000, and abandoned on February 14, 2003. However, the present application is not copending with the prior application. Additionally, the present application also appears not to be claiming priority to any application which also meets the requirements (reference, copendency, and a common inventor) for priority to this earlier application. The applicant is therefore not accorded benefit to the earlier filing date of the 09/710,059 application.

5. As indicated above, the Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120. The reference to the earlier application indicates above must be submitted during the pendency of the later-filed application. If the later-filed application is an application filed under 35 U.S.C. 111(a), this reference must

also be submitted within the later of four months from the actual filing date of the later-filed application or sixteen months from the filing date of the prior-filed application. If the later-filed application is a nonprovisional application which entered the national stage from an international application after compliance with 35 U.S.C. 371, this reference must also be submitted within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371 (b) or (f) in the later-filed international application or sixteen months from the filing date of the prior-filed application. These time periods are not extendable. Except as provided in paragraph (a)(3) of this section, the failure to timely submit the reference required by 35 U.S.C. 120 and paragraph (a)(2)(i) of this section is considered a waiver of any benefit under 35 U.S.C. 120, 121, or 365(c) to such prior-filed application.

A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional.

Specification

6. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification does not provide antecedent basis support for the genus of methods indicated in claim 3 (i.e. there is no antecedent basis support in the description for

methods of using PDZ domain polypeptides that bind E6 proteins encoded by HPV strains 16, 18, and 45).

Claim Objections

7. Claims 1, 7, and 0 are objected to because of the following informalities: each of these claims refer to the human papillomavirus in the first instance as HPV, without first identifying the virus by its complete name. It is suggested that the claim be amended such that the first instance of the term "HPV" reads instead as - -human papillomavirus (HPV)- -. Appropriate correction is required.

8. Claim 3 is objected to because of the following informalities: the claim provides a list of HPV strains in line 2. It is suggested that a comma be inserted between the last two members of the list so that the claim identifies strains - - 16, 18, and 45- -. Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, and 3-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of detecting the presence of an oncogenic HPV by contacting a sample with the Magi-I PDZ domain 2, does not reasonably provide enablement

for methods of using any PDZ domain polypeptide for the detection of any oncogenic HPV or HPV E6 protein in the sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims read on methods for the detection of oncogenic HPV E6 protein in a sample, or infection by an oncogenic EPV, by contacting the sample with any PDZ domain polypeptide, including a polypeptide comprising the Magi-I PDZ domain 2.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

As indicated above, the present claims are drawn broadly to methods of detecting any oncogenic HPV E6 protein using any PDZ domain containing polypeptide (also referred to as PDZ polypeptides and PDA domain polypeptides). Other of the indicated claims limit the PDZ domain polypeptides to those comprising the Magi-I PDZ domain 2, or to embodiments wherein the PDZ polypeptide binds to the E6 proteins of each of HPV strains 16, 18, and 45.

In support of these claims, the application discloses a number of PDZ domain polypeptides (pages 27-36), and identifies some such polypeptides that interact with some oncogenic HPV E6 proteins (pages 88-89). The application does not demonstrate that every oncogenic E6 protein is able to bind every PDZ domain polypeptide, or identify any means of determining in advance which PDZ domains are likely to bind to any given E6 protein, with the possible exception of the Magi-I PDZ domain 2 which appears to bind to each of the oncogenic E6 proteins tested.

The art supports the teachings of the application insofar as they indicate that oncogenic E6 proteins target the Magi-I PDZ domain 2. See e.g., Glaunsinger et al., Oncogene 19: 5270-80 (of record in the September 2003 IDS). However, the art also indicates that the interaction between PDZ polypeptides and PDZ binding polypeptides is dependant not only on the presence of a PDZ and PDZ-binding motif, but also on other sequence requirements resulting in specificity of binding between the two polypeptides. See e.g., Glaunsinger, page 5277 right column (stating "that precise sequence requirements both within the PDZ domain-binding motif ... and within each PDZ domain ... determine these highly specific protein-protein interactions"). The reference also demonstrates that PDZ-binding proteins, both that referred to as the adenovirus 9ORF1 oncoprotein and the HPV E6 oncoproteins, are able to bind some PDZ-proteins and not others (page 5277, left column). Additionally, Glaunsinger further teaches that the 9ORF1 protein interacts only with specific PDZ domains within a specific PDZ-domain containing protein, and not with every PDZ-domain therein (page 5273, right column). From these references, it is apparent that any given PDZ-binding protein, such as the HPV E6 protein, is able to bind only to certain PDZ domain sequences. These teachings are evidenced by the

teachings on pages 88-89 of the present application, demonstrating that, with the exception of Magi-I domain 2 binding, the PDZ-domain binding specificities of different E6 proteins are not identical. Thus, the art is complex, and unpredictable, in that those in the art must be able to determine which PDZ-binding domains interact with what PDZ domain sequences, and that there does not appear to be any means of predicting such interaction absent large scale testing for protein-protein interactions.

In order to practice the claimed methods to the full extent, those in the art would be required to determine for themselves which PDZ domain sequences are bound by any given E6 protein. In view of the complexity and unpredictability in the art of making such determinations; the limited examples, and lack of any established predictive formula, provided by the application; and the breadth of the claims, the application has not provided sufficient information to enable those in the art to practice the claimed methods to the full extent claimed without undue experimentation.

11. Claims 1, 3-8, 10-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims have been described above. Each of the claims is drawn, inherently or explicitly, to methods of using a PDZ domain polypeptide that is able to bind to an oncogenic E6 polypeptide. Thus, the claims are drawn to methods of using a genus of

polypeptides comprising a PDZ domain, and having the ability to bind to oncogenic HPV E6 polypeptides.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

In the present case, the application teaches certain PDZ binding polypeptides that are capable of binding to certain oncogenic HPV E6 proteins. Page 88-89. However, the application does not teach that this is a complete list of all PDZ polypeptides that bind to the indicated E6 proteins. Additionally, as can be seen from the teachings on pages 88-89, different E6 proteins appear to interact with a different set of PDZ polypeptides. Further, there is no apparent common structure to the different PDZ polypeptides that distinguishes the PDZ polypeptides that bind to any given E6 protein from those that do not. There is therefore a high level of uncertainty as to which PDZ polypeptides would fall within the scope of the indicated genus of PDZ polypeptides

that bind to oncogenic HPV E6 proteins. See also, the teachings of Glaunsinger et al., supra (indicating complexity and unpredictability in the art). In view of the fact that the examples provided do not demonstrate possession of the genus encompassing every PDZ domain polypeptide that binds any oncogenic E6 protein, and that the application has identified no structure correlating with the PDZ polypeptides' ability to bind these E6 proteins, there is insufficient written description support for the indicated genus of PDZ polypeptides, and therefore for the methods of using them.

12. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This claim reads on methods of detecting oncogenic HPV or HPV E6 proteins comprising the use of any PDZ domain polypeptide as a E6 binding protein. In particular, this claim is directed to embodiments wherein the PDZ domain polypeptide "binds to HPV E6 protein encoded by HPV strains 16, 18, and 45." Thus, the claim reads on methods of using any PDZ domain polypeptide falling within the genus of PDZ domain polypeptides that bind the E6 proteins of each of HPV strains 16, 18, and 45.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical

> and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

In the present case, the Applicant has identified the PDZ domain polypeptides useful in the claimed methods only by function: the ability to bind the E6 proteins of the three identified HPV strains. However, while the application identifies several PDZ domain polypeptides (pages 27-36, Table 2), and identifies some of these polypeptides that are able to bind to the E6 proteins of certain HPV strains (pages 88-89, Table 4), it does not identify every PDZ domain polypeptide that binds to each of the three identified HPV strains. It is noted that the application identified two PDZ polypeptides that bind to each of HPV strains 16 and 18. However, it does not provide a similar list for PDZ polypeptides that bind to HPV strain 45. Thus, the application does not identify species clearly within the claimed genus.

Nor does the application provide a specific structure of the PDZ polypeptides within the genus that correlates with the required function. Because there is no identification of structures common to each PDZ polypeptide that binds all three E6 proteins, nor sufficient representative examples of the PDZ polypeptides by which such a structure may be determined, the application also fails to provide sufficient written description support for the identified genus of PDZ

polypeptides through identification of a structure and function. While all of the polypeptides are required to have a PDZ domain, this is not alone sufficient structure to correlate with the function. This is because, as indicated by the variation of PDZ polypeptide binding to E6 proteins in Table 4, the mere presence of a PDZ domain does not demonstrate that a polypeptide would be able to bind to the E6 protein. Rather, the Table shows that the binding between PDZ polypeptides and E6 proteins varies both with the specific PDZ polypeptide and with the specific strain of HPV from which the E6 protein is derived.

For the reasons above, and in view of the uncertainty as to which PDZ polypeptides would be able to bind the three identified HPV E6 proteins, the application has not provided sufficient written description support for the use of the genus of PDZ domain polypeptides identified in claim 3. The application therefore fails to provide adequate support for methods of using this genus of polypeptides.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1, 4-8, 10-13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Davis et al. (U.S. 5610,077- of record in the May 2004 IDS) in view of Bleul et al. (U.S. 5,753,233- of record in the September 2003 IDS) and either of Kiyono et al.

(PNAS 94: 11612-16) or Gardiol et al. (Oncogene 18: 5487-96- of record in the May 2004 IDS). These claims are drawn to methods of detecting infection by oncogenic HPV, or the E6 proteins of such virus, by contacting a sample suspected of containing such a molecule with 1) a PDZ domain polypeptide and (optionally) 2) an antibody that binds to the E6 protein. The claims also include embodiments wherein the PDZ domain or the antibody is labeled (including where the PDZ polypeptide is a fusion polypeptide). The application defines a PDZ domain polypeptide as any polypeptide, without limit as to size, comprising a PDZ domain. Page 8. Thus, the claims read on methods of using any PDZ domain containing polypeptide for use in the detection of oncogenic HPV infection or oncogenic HPV E6 proteins.

Davis teaches methods for the detection of analytes comprising two binding partners to an intended analyte. Abstract, column 2, Although the reference indicates that the binding partner in the preferred embodiments are antibodies (e.g., column 2 lines 58-67), the teachings of the patent would have rendered it obvious to those in the art that any binding partner to the intended analyte may be used. The reference further teaches the use of labels conjugated to the binding partners. Column 2 lines 31-35. However, the reference does not teach the use of such an assay to specifically detect HPV E6 proteins, or the use of a PDZ polypeptide as a binding partner to the E6 protein.

Bleul teaches the diagnosis of HPV, or the detection of HPV polypeptides in a sample, through use of antibodies directed against the HPV E6 protein. Column 2, lines 5-16. From these teachings, it would have been obvious to those in the art to use a method such as those described in Davis for the detection of the oncogenic E6 protein (and therefore to determine HPV infection). Also, it would have been obvious to those in the art to use antibodies directed against

the E6 protein as at least one of the E6 protein binding partners. See also, Guiot et al., Cancer Cells 7: 193-96, e.g. abstract (of record in the May 2004 IDS- teaching the use of antibodies against the E6 proteins as a means of detecting the E6 proteins in samples, and thereby diagnosing infection by HPV).

Kiyono teaches that certain PDZ polypeptides are specifically bound by oncogenic E6 polypeptides. It would therefore have been obvious to those in the art to use such PDZ polypeptides as a binding partner for the detection of HPV E6 proteins in a method such as those disclosed by Davis. Further, from the teachings of Kiyono and Davis, it would have been obvious to those in the art the PDZ polypeptides could be produced as a fusion protein with a detectable marker (e.g. the enzyme GST) for use in methods of detection. See e.g., Lee et al., PNAS 94: 6670-75, pages 6670-71 (of record in the September 2003 IDS). The Gardiol reference provides similar teachings to those of Kiyono. See e.g., pages 5487 –89 and 5494-95. Because the Kiyono and Gardiol references teach that the disclosed PDZ polypeptides are bound by a domain found on oncogenic HPV E6 proteins, but not other HPV E6 proteins, it would have been obvious to those in the art that such PDZ polypeptides could be used in the detection of the oncogenic HPV E6 proteins. The combined teachings of these references therefore render the claimed inventions obvious.

15. Claims 1, 4-8, 10-13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Davis in view of Bleul and Lee et al. (PNAS 94: 6670-75- of record in the September 2003 IDS). The claims have been described above, as have the teachings of both Davis and Bleul. The Lee reference teaches that the PDZ containing protein DLG binds to the C-

terminal of high-risk HPV E6 proteins, but not to low-risk HPV proteins. Page 6674. From these teachings, it would have been obvious to use the PDZ protein DLG as a binging partner for use in detection of oncogenic E6 proteins as suggested by the teachings of Davis and Bleul. The combined teachings of these references therefore render the claimed inventions obvious.

16. Claims 1-13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Davis in view of Glaunsinger et al. (Oncogene 19: 5270-80) and Bleul. The claims have been described above, except that claim 2 further requires that the PDZ polypeptide is comprises the Magi-I PDZ domain 2 sequence, and claim 3 requires that the PDZ polypeptides binds to the E6 proteins of each of HPV strains 16, 18, and 45. It is noted that, because the Magi-I PDZ domain appears to bind to the C-terminal of all oncogenic HPV proteins, the limitation of claim 3 would be inherent in the use of Magi-I PDZ domain 2 for the detection of oncogenic HPV E6 proteins. The teachings of each of the Davis and Bleul references have also been described above. Glaunsinger provides teachings substantially similar to those of the Kiyono reference, except that the reference identifies the Magi-I protein as a PDZ polypeptide which is bound by the oncogenic HPV E6 proteins. Page 5277. The reference also teaches that the Magi-I protein, and the PDZ domains thereof, may be expressed as fusion proteins with a label. Page 5279. It would therefore have been obvious to those in the art to use the Magi-I protein as a binding partner in the methods suggested by Davis and Bleul.

17. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Davis in view of Bleul and any of Gardiol, Kiyono, or Glaunsinger as applied above, and further in view of

Kehmeier et al. (Virology 299: 72-87). This claim further limits the previously described methods to embodiments wherein the sample to be tested for the presence of the oncogenic E6 protein is prepared in the presence of a proteasome inhibitor. It is noted that the current application claims priority to applications filed prior to the Kehmeier reference. However, none of these prior applications appears to provide support for methods of detecting HPV using a PDZ polypeptide wherein the sample tested is prepared using a proteasome inhibitor. Thus, the Applicant is not afforded priority to these earlier applications with respect to the limitations of claim 14.

The teachings of the Davis, Bleul, Glaunsinger, and Kiyono references have been described above. While the teachings of these references suggest the use of certain PDZ polypeptides in methods for the detection of oncogenic HPV E6 proteins, they do not teach or suggest the preparation of samples to be tested in the presence of a proteasome inhibitor. However, the Kehmeier reference teaches the steady state levels of oncogenic E6 proteins in cells can be increased when the cells are provided with proteasome inhibitors. See e.g., page 73. Because those in the art would be motivated to increase the yield of the oncogenic E6 proteins in a sample so as to have better results in testing for the proteins' presence, those in the art would also be motivated to prepare the sample in the presence of a proteasome inhibitor as was described by the Kehmeier reference. The teachings of this reference, in combination with those previously cited, therefore renders the claimed methods obvious.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 8, 9, 10 of copending Application No. 10/847,818. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending application are generic to the presently claimed methods. However, the currently claimed methods are obvious variations of the methods in the copending application based on the teachings of (e.g.) pages 123-27 of that application. Because the present application is an obvious variation of the claims of the copending application, the present claims are provisionally rejected for obviousness type double patenting.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. The above rejection is, in part, based on the specification of a previously issued patent, rather than the claims. In support of the use of this material, the examiner notes the following excerpt from MPEP section 804 II(B)(1):

> When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. This does not mean that one is precluded from all use of the patent disclosure.
>
> The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in Vogel recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court, one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

Thus, the courts have held that it is permissible to use the specification in determining what is included in, and obvious from, the invention defined by the claim on which the rejection is based. This is true even where elements are drawn from the specification describing the claimed invention which are not elements in the claim itself.

Conclusion

21. No claims are allowed.

22. The following prior art references are made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> Band et al., U.S. Patent 6,440,696. This reference provides teachings similar to those of the Lee reference described above. See e.g., columns 51-52. The reference is considered redundant to the teachings of Lee, Kiyono, and Gardiol.
>
> Thomas et al., Oncogene, 20: 5431-39. This reference is considered redundant to those of the Glaunsinger et al. reference above.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 2/7/05
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600